(FILE 'HOME' ENTERED AT 12:06:15 ON 15 OCT 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS, MEDICONF' ENTERED AT 12:06:26 ON 15 OCT 2002

L1 10 S (CALCIUM OR TRICALCIUM)(L)CYRSTALL?
L2 10 DUP REM L1 (0 DUPLICATES REMOVED)
L3 10 SORT L2 PY
E PAULISTA M?/AU
L4 12 S E4
L5 12 DUP REM L4 (0 DUPLICATES REMOVED)
L6 12 SORT L5 PY

=> d an ti so au ab pi l6 1-10

L6 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1995:464505 CAPLUS
DN 122:231763
TI A new growth/differentiation factor from the transforming growth factor .beta. family
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
IN Hoetten, Gertrud; Neidhardt, Helge; **Paulista, Michael**
AB A new member of the TGF-.beta. family of growth/differentiation factors (MP-52) and a cDNA and the gene encoding it are described. A partial cDNA was obtained by PCR using amino acid sequence-derived primers and this was used to screen a com. human gene bank to obtain the gene. Expression of the cDNA in animal cells is using vaccinia and bovine papillomavirus vectors is demonstrated. The protein was found to have.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4420157	A1	19950223	DE 1994-4420157	19940609
CA 2169171	AA	19950216	CA 1994-2169171	19940809
WO 9504819	A1	19950216	WO 1994-EP2630	19940809
W: AU, BY, CA, CN, CZ, HU, JP, KR, LT, NZ, RU, SI, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9474986	A1	19950228	AU 1994-74986	19940809
AU 688362	B2	19980312		
EP 713529	A1	19960529	EP 1994-924856	19940809
EP 713529	B1	20000202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1129013	A	19960814	CN 1994-193027	19940809
HU 74271	A2	19961128	HU 1995-3853	19940809
HU 219504	B	20010428		
JP 09501053	T2	19970204	JP 1994-506226	19940809
AT 189475	E	20000215	AT 1994-924856	19940809
ES 2142953	T3	20000501	ES 1994-924856	19940809
RU 2157406	C2	20001010	RU 1996-104372	19940809
CZ 288795	B6	20010912	CZ 1996-357	19940809
ZA 9405992	A	19950314	ZA 1994-5992	19940810
US 5994094	A	19991130	US 1994-288508	19940810
TW 448183	B	20010801	TW 1994-83108337	19940909

L6 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1997:502239 CAPLUS
DN 127:113356
TI Targeted proteins with cartilage- and/or bone-inducing activity
SO Ger. Offen., 13 pp.
CODEN: GWXXBX
IN Hoetten, Gertrud; Bechtold, Rolf; Pohl, Jens; **Paulista, Michael**
AB Proteins of the TGF-.beta. superfamily with cartilage- and/or bone-inducing activity or fragments thereof are conjugated, optionally through a spacer, with ligands possessing affinity (1) for the extracellular matrix and/or cellular components of cartilage and/or bone, (2) for a biocompatible carrier matrix for joint or bone implants, or (3) for a bone adhesive. The spacer groups are preferably peptides; the ligands may be peptides or diphosphonates. Pharmaceutical compns. contg. these conjugates are useful for treatment and prevention of bone and cartilage damage and diseases such as osteoporosis, Paget's disease, osteodystrophy, osteoarthritis, or osteoarthropathy (no data). Their

action may be enhanced by addn. of agents which inhibit bone resorption. The protein of the conjugate may be produced by recombinant DNA technol.; sequences of a suitable protein and of the encoding DNA are provided.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19548476	A1	19970626	DE 1995-19548476	19951222
	WO 9723612	A2	19970703	WO 1996-EP5768	19961220
	WO 9723612	A3	19970828		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9713037	A1	19970717	AU 1997-13037	19961220

L6 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1997:145191 CAPLUS
DN 126:139895
TI Use of protein MP52 for prevention and treatment of nervous system disorders
SO Ger. Offen., 21 pp.
CODEN: GWXXBX
IN Hoetten, Gertrud; Pohl, Jens; Bechtold, Rolf; **Paulista, Michael**; Unsicker, Klaus
AB Protein MP52, a growth and differentiation factor of the TGF-.beta. superfamily, and fragments and fusion proteins thereof are useful for prevention and treatment of nervous system disorders and neuropathol. conditions caused by aging of the nervous system. MP52 improves the survival of dopaminergic neurons, at least partially through an action on the assocd. astrocytes. Thus, MP52 DNA on a vaccinia virus vector was expressed in 143B cells, and MP52 DNA on prokaryotic vector pBP2 was expressed in Escherichia coli, purified by reversed-phase HPLC, and refolded at pH 8-10. Transcription of MP52 DNA was obsd. in mouse brain and rat spinal cord.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19525416	A1	19970116	DE 1995-19525416	19950712
	WO 9703188	A2	19970130	WO 1996-EP3065	19960712
	WO 9703188	A3	19970227		
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	AU 9666151	A1	19970210	AU 1996-66151	19960712
	EP 837938	A2	19980429	EP 1996-925740	19960712
	R: DE, ES, FR, GB, IT				
	JP 11509097	T2	19990817	JP 1996-505511	19960712
	US 2002045568	A1	20020418	US 1998-981490	19980518

L6 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1998:774377 CAPLUS
DN 130:12138
TI Self-replicating agent in pharmaceutical composition and diagnostic kit directed to a heterologeneous pathogenic organism in a host
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
IN Pohl, Jens; Bechtold, Rolf; **Paulista, Michael**; Dill, Othmar
AB The present invention relates to a pharmaceutical compn. comprising a self-replicating agent directed to a heterologeneous pathogenic organism in a host, and to a process for its prepn. Further, the present invention relates to a diagnostic kit comprising the self-replicating agent. The agent is a bacteriophage.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9851318	A1	19981119	WO 1998-EP2871	19980515

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9881043	A1	19981208	AU 1998-81043	19980515
EP 983077	A1	20000308	EP 1998-930692	19980515

R: CH, DE, ES, FR, GB, IT, LI

L6 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1998:721462 CAPLUS
DN 129:326984
TI Cloning and cDNA sequence encoding a human protein phosphatase
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
IN Hanke, Michael; **Paulista, Michael**; Pohl, Jens
AB The present invention relates to nucleic acids encoding a novel human protein phosphatase (MP-19) of the family of protein serine/threonine phosphatases. In particular, it relates to novel DNA sequences encoding serine/threonine protein phosphatase, to expression plasmids contg. said nucleic acids, to host organisms transformed by said expression plasmids, to the prodn. of said protein by culturing said transformant, to antibodies specifically binding to said phosphatase and to agonists and/or antagonists for said protein, and to antisense MP-19 nucleic acid. Amino acid sequence alignment of MP-19 with sequences of different protein phosphatase 2C enzymes demonstrates the homol. of MP-19 to the PP2C family but implicates also that MP-19 belongs to a new protein phosphatase group. A preferred substrate for the PP2C-like protein is the SET protein, suggesting capacities possibly relevant to therapeutic treatment of leukemia; MP-19 also prefers basic substrates such as histones, and MBP phosphorylated by cAMP-dependent protein kinase, suggesting a special function for this phosphatase in the brain. Predominant expression of MP-19 was detected in human testis, with lower expression in human pituitary, gland, thymus, small intestine, and fetal liver, and basal expression found in all other human samples. Furthermore, the invention relates to serine or threonine residues and epitopes comprising said residues dephosphorylated by said protein and pharmaceutical compns. comprising said protein or agonists or antagonists thereof for the treatment of diseases influenced by changes in phosphorylation which controls e.g. cell proliferation and/or differentiation, to diagnostic kits and to in vitro diagnostic methods for the detection of phosphorylation dependent diseases such as e.g. cancer.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 874052	A2	19981028	EP 1998-107346	19980422
EP 874052	A3	19990224		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

L6 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1998:335063 CAPLUS
DN 129:32362
TI Compositions with improved cartilage- and/or bone-inducing activity
SO Ger. Offen., 12 pp.
CODEN: GWXXBX
IN **Paulista, Michael**; Pohl, Jens; Pabst, Joachim; Heide, Helmut
AB A bioactive implant material with cartilage- and/or bone-inducing activity comprises (A) s bone- and/or cartilage-inducing protein or protein mixt. and (B) a microporous Ca phosphate ceramic carrier matrix with interconnecting pores, which has inherent bone-inducing activity. The inducing protein preferably belongs to the TGF-.beta. superfamily, esp. protein MP52. The implant material is useful for treatment of cartilage and/or bone damage or diseases (no data).

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19647853	A1	19980520	DE 1996-19647853	19961119
WO 9821972	A2	19980528	WO 1997-EP6463	19971119

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9855533	A1	19980610	AU 1998-55533	19971119
EP 942758	A2	19990922	EP 1997-951919	19971119
R: DE, ES, FR, GB, IT				
JP 2001505097	T2	20010417	JP 1998-523215	19971119

L6 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1998:106003 CAPLUS
DN 128:163251
TI A growth factor from chromaffin granules that acts as a glial cell neurotrophic factor and promotes survival of dopaminergic neurons
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
IN Unsicker, Klaus; **Paulista, Michael**; Pohl, Jens; Bechtold, Rolf
AB Chromaffin granule-derived epidermal growth factor-like proteins that promote survival of dopaminergic neurons and of astrocytes are identified and characterized for use in the treatment of disease affecting dopaminergic neurons. These factors or derivs. or analogs that may be of therapeutic use. Solubilized bovine chromaffin granules promoted the in vitro survival of dopaminergic neurons and of astroglia. Treatment of chromaffin granules with carbachol released the factor responsible for this effect. The factor also protected dopaminergic neurons against MPP+ toxicity. The effect was not due to known neuropeptides from chromaffin granules and it could be blocked with an antagonist of the EGF receptor superfamily tyrosine kinase (dianilinophthalimide).

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9804688	A1	19980205	WO 1997-EP4087	19970728

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9742028	A1	19980220	AU 1997-42028	19970728
EP 922101	A1	19990616	EP 1997-940036	19970728
R: DE, ES, FR, GB, IT				
JP 2000516457	T2	20001212	JP 1998-508507	19970728

L6 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1999:231521 CAPLUS
DN 130:251235
TI Cytokines having neurotrophic activity
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
IN Unsicker, Klaus; Pohl, Jens; **Paulista, Michael**; Bechtold, Rolf
AB The present invention relates to a pharmaceutical compn. having neurotrophic activity, comprising a biol. active amt. of at least two cytokines, wherein at least one of said cytokines is bone morphogenetic proteins (BMP), growth differentiation factor (GDF), TGF-.beta. or glial cell line-derived neurotrophic-like factors (GDNF). The cytokines and pharmaceutical compns. contg. them are useful for treating peripheral and/or CNS disorders (Alzheimer's disease, Parkinson's disease, dementia, neurodegenerative disease, diabetes, cisplatinium) in mammals.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9915191	A2	19990401	WO 1998-EP6004	19980921
WO 9915191	A3	19990520		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2301693	AA	19990401	CA 1998-2301693	19980921
AU 9910248	A1	19990412	AU 1999-10248	19980921
EP 1011712	A2	20000628	EP 1998-952613	19980921
R: DE, ES, FR, GB, IT				
JP 2001517634	T2	20011009	JP 2000-512560	19980921

L6 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:290658 BIOSIS
TI Growth/differentiation factor of the TGF-beta family.
SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 30, 1999) Vol. 1228, No. 5, pp. No pagination. e-file.
ISSN: 0098-1133.
AU Hotten, Gertrud (1); Neidhardt, Helge; **Paulista, Michael**
AB The invention concerns a protein of the TGF-beta family, the DNA coding therefor and a pharmaceutical composition containing the protein.
PI US 5994094 November 30, 1999

L6 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:319747 CAPLUS
DN 134:331637
TI Use of GDNF for treating corneal defects
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
IN Hanke, Michael; Kruse, Friedrich; **Paulista, Michael**; Pohl, Jens
AB The present invention relates to the use of a glial cell line-derived growth factor (GDNF) or a functionally active deriv. or part thereof and/or an agonist which substitutes the functional activity of GDNF, and/or a nucleic acid contg. at least a nucleotide sequence encoding the primary amino acid sequence of GDNF or the functionally active deriv. or part thereof and/or of the agonist for the manuf. of a pharmaceutical compn. for epidermal and stromal wound healing.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001030375	A2	20010503	WO 2000-EP10674	20001030
WO 2001030375	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1223966	A2	20020724	EP 2000-983097	20001030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

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     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS,
     MEDICONF' ENTERED AT 12:06:26 ON 15 OCT 2002
L1            10 S (CALCIUM OR TRICALCIUM)(L)CYRSTALL?
L2            10 DUP REM L1 (0 DUPLICATES REMOVED)
L3            10 SORT L2 PY
                 E PAULISTA M?/AU
L4            12 S E4
L5            12 DUP REM L4 (0 DUPLICATES REMOVED)
L6            12 SORT L5 PY

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L6   ANSWER 6 OF 12  CAPLUS  COPYRIGHT 2002 ACS
AN   1998:335063  CAPLUS
DN   129:32362
TI   Compositions with improved cartilage- and/or bone-inducing activity
IN   Paulista, Michael; Pohl, Jens; Pabst, Joachim; Heide, Helmut
PA   Biopharm Gesellschaft zur biotechnologischen Entwicklung von Pharmaka
     m.b.H., Germany; GerontoCare G.m.b.H. Biomaterials und Medical Devices
SO   Ger. Offen., 12 pp.
     CODEN: GWXXBX
DT   Patent
LA   German
IC   ICM  A61L027-00
     ICS  C07K017-14; C07K014-495; A61K038-18; A61K006-00
CC   63-7 (Pharmaceuticals)
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   DE 19647853        A1   19980520       DE 1996-19647853 19961119
     WO 9821972         A2   19980528       WO 1997-EP6463   19971119
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
             US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9855533         A1   19980610       AU 1998-55533    19971119
     EP 942758          A2   19990922       EP 1997-951919   19971119
         R:  DE, ES, FR, GB, IT
     JP 2001505097      T2   20010417       JP 1998-523215   19971119
PRAI DE 1996-19647853   A    19961119
     WO 1997-EP6463     W    19971119
AB   A bioactive implant material with cartilage- and/or bone-inducing activity
     comprises (A) s bone- and/or cartilage-inducing protein or protein mixt.
     and (B) a microporous Ca phosphate ceramic carrier matrix with
     interconnecting pores, which has inherent bone-inducing activity.  The
     inducing protein preferably belongs to the TGF-.beta. superfamily, esp.
     protein MP52.  The implant material is useful for treatment of cartilage
     and/or bone damage or diseases (no data).
ST   cartilage induction implant TGF beta; bone induction protein MP52 implant;
     calcium phosphate implant bone induction
IT   Bone
        (artificial; compns. with improved cartilage- and/or bone-inducing
        activity)
IT   Biodegradable materials
        (carriers; compns. with improved cartilage- and/or bone-inducing
        activity)
IT   Musculoskeletal diseases
     Musculoskeletal diseases
        (cartilage; compns. with improved cartilage- and/or bone-inducing
        activity)
IT   Bone, disease
     Bone formation
     Cartilage
     Immobilization
```

(compns. with improved cartilage- and/or bone-inducing activity)

IT Bone morphogenetic proteins
Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. with improved cartilage- and/or bone-inducing activity)

IT Cartilage
Cartilage
(degeneration; compns. with improved cartilage- and/or bone-inducing activity)

IT Jaw
(disease, odontogenic cyst; compns. with improved cartilage- and/or bone-inducing activity)

IT Cartilage
Cartilage
(disease; compns. with improved cartilage- and/or bone-inducing activity)

IT Bone, disease
(fracture; compns. with improved cartilage- and/or bone-inducing activity)

IT Prosthetic materials and Prosthetics
(implants; compns. with improved cartilage- and/or bone-inducing activity)

IT Bone, disease
Bone, disease
(injury; compns. with improved cartilage- and/or bone-inducing activity)

IT Porous materials
(microporous, implants; compns. with improved cartilage- and/or bone-inducing activity)

IT Jaw
(odontogenic cyst; compns. with improved cartilage- and/or bone-inducing activity)

IT Periodontium
(periodontitis; compns. with improved cartilage- and/or bone-inducing activity)

IT Surgery
(plastic; compns. with improved cartilage- and/or bone-inducing activity)

IT Fusion proteins (chimeric proteins)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(with TGF-.beta. superfamily proteins; compns. with improved cartilage- and/or bone-inducing activity)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-, superfamily; compns. with improved cartilage- and/or bone-inducing activity)

IT 10103-46-5 159994-86-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. with improved cartilage- and/or bone-inducing activity)

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13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2002:505399 CAPLUS
DN 137:75061
TI Mammalian osteoblast/chondrocyte protein OCP and Adlican genes associated with mechanical stress
SO U.S. Pat. Appl. Publ., 198 pp., Cont.-in-part of U. S. Ser. No. 729,485. CODEN: USXXCO
IN Einat, Paz; Segev, Orit; Skaliter, Rami; Feinstein, Elena; Faerman, Alexander
AB The disclosure relates to mech. stress induced genes, such as those from human and from mice and rats, and their expressed proteins. A novel gene CMF608 (OCP) is discovered, the expression of which is upregulated by mech. stress on primary calvaria cells. Several functional features identify OCP as the most specific early marker of osteo- or chondro-progenitor cells as well as an inducer of osteoblast proliferation and differentiation. The terminal differentiation of osteoblasts and chondrocytes appears to be accompanied by down-regulation of OCP expression. DNA sequences are provided for human, rat, and mouse cDNAs, genes, and promoters for the OCP proteins. Homol. between rat and human N-terminal portions of the OCP protein is esp. significant within the first 250 amino acids. Adlican is a recently described proteoglycan derived from placenta with leucine-rich repeats and Ig regions similar to those of the OCP protein. The invention also provides probes therefor, tests to identify such genes, uses for such genes and expression products, e.g., in diagnosis (for instance risk detn.), treatment, prevention, or control, of osteoporosis or factors or processes which lead to osteoporosis; and, to diagnostic, treatment, prevention, or control methods or processes, as well as compns. therefor and methods or processes for making and using such compns.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002086825	A1	20020704	US 2001-802318	20010308
	US 2002022026	A1	20020221	US 2000-729485	20001204
	US 2002037511	A1	20020328	US 2001-792471	20010223
	US 2002137705	A1	20020926	US 2001-905129	20010713
	WO 2002046364	A2	20020613	WO 2001-US46400	20011204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

(FILE 'HOME' ENTERED AT 12:06:15 ON 15 OCT 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS, MEDICONF' ENTERED AT 12:06:26 ON 15 OCT 2002

L1	10	S (CALCIUM OR TRICALCIUM)(L)CYRSTALL?
L2	10	DUP REM L1 (0 DUPLICATES REMOVED)
L3	10	SORT L2 PY
		E PAULISTA M?/AU
L4	12	S E4
L5	12	DUP REM L4 (0 DUPLICATES REMOVED)
L6	12	SORT L5 PY
L7	477	S MATRIX (L) TRICALCIUM
L8	7	S L7 AND CRYSTALLO?
L9	5	DUP REM L8 (2 DUPLICATES REMOVED)
L10	5	SORT L9 PY
L11	0	S L7 AND MP52
L12	1078	S PERIODONTOSIS
L13	1	S L12 AND (GENE THERAPY)
L14	0	S L12 AND MP52

ILE 'HOME' ENTERED AT 14:03:46 ON 15 OCT 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS, MEDICONF' ENTERED AT 14:03:52 ON 15 OCT 2002

L1 36 S MP52
L2 36 DUP REM L1 (0 DUPLICATES REMOVED)
L3 36 SORT L2 PY
L4 21 S L3 AND (BONE OR CARTILAGE)
L5 21 SORT L4 PY

=> d an ti so au ab pi l5 10 1 2 3 6 9 12

L5 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1998:335063 CAPLUS
DN 129:32362
TI Compositions with improved **cartilage**- and/or **bone** -inducing activity
SO Ger. Offen., 12 pp.
CODEN: GWXXBX
IN Paulista, Michael; Pohl, Jens; Pabst, Joachim; Heide, Helmut
AB A bioactive implant material with **cartilage**- and/or **bone** -inducing activity comprises (A) s **bone**- and/or **cartilage**-inducing protein or protein mixt. and (B) a microporous Ca phosphate ceramic carrier matrix with interconnecting pores, which has inherent **bone**-inducing activity. The inducing protein preferably belongs to the TGF-.beta. superfamily, esp. protein **MP52**. The implant material is useful for treatment of **cartilage** and/or **bone** damage or diseases (no data).

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19647853	A1	19980520	DE 1996-19647853	19961119
WO 9821972	A2	19980528	WO 1997-EP6463	19971119
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9855533	A1	19980610	AU 1998-55533	19971119
EP 942758	A2	19990922	EP 1997-951919	19971119
R: DE, ES, FR, GB, IT				
JP 2001505097	T2	20010417	JP 1998-523215	19971119

L5 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1993:664168 CAPLUS
DN 119:264168
TI Novel human growth/differentiation factors, cloning and expression of cDNA for these factors, and use of the factors and antibodies to these factors in pharmaceuticals and in diagnosis
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
IN Neidhardt, Helge; Hoetten, Gertrud
AB The cDNAs for proteins of the TGF-.beta. family from human liver (MP-121) and embryo (MP-52) are cloned and sequenced. These factors may be used in treatment of various **bone**, **cartilage**, and tooth defects and in wound and tissue repair processes (no data). Antibodies to the factors can be used in diagnosis (no data). PCR primers used to amplify the cDNA for MP-52 and MP-121 were prepd. based on comparisons of DNA sequences encoding TGF-.beta.'s, inhibins, and **bone** morphogenetic proteins.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9316099	A2	19930819	WO 1993-EP350	19930212
WO 9316099	A3	19930930		
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,				

BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9334971	A1	19930903	AU 1993-34971	19930212
AU 666170	B2	19960201		
EP 625989	A1	19941130	EP 1993-903966	19930212
EP 625989	B1	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
JP 07503847	T2	19950427	JP 1993-513793	19930212
JP 3193050	B2	20010730		
HU 67683	A2	19950428	HU 1994-2143	19930212
HU 218845	B	20001228		
JP 09182593	A2	19970715	JP 1996-288766	19930212
AT 188996	E	20000215	AT 1993-903966	19930212
ES 2141761	T3	20000401	ES 1993-903966	19930212
CZ 287715	B6	20010117	CZ 1994-1942	19930212
US 6120760	A	20000919	US 1994-289222	19940812
CZ 287810	B6	20010214	CZ 1997-1069	19970408
US 6197550	B1	20010306	US 1998-54526	19980403

L5 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1995:464505 CAPLUS
DN 122:231763
TI A new growth/differentiation factor from the transforming growth factor .beta. family
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
IN Hoetten, Gertrud; Neidhardt, Helge; Paulista, Michael
AB A new member of the TGF-.beta. family of growth/differentiation factors (MP-52) and a cDNA and the gene encoding it are described. A partial cDNA was obtained by PCR using amino acid sequence-derived primers and this was used to screen a com. human gene bank to obtain the gene. Expression of the cDNA in animal cells is using vaccinia and bovine papillomavirus vectors is demonstrated. The protein was found to have.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4420157	A1	19950223	DE 1994-4420157	19940609
CA 2169171	AA	19950216	CA 1994-2169171	19940809
WO 9504819	A1	19950216	WO 1994-EP2630	19940809
W: AU, BY, CA, CN, CZ, HU, JP, KR, LT, NZ, RU, SI, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9474986	A1	19950228	AU 1994-74986	19940809
AU 688362	B2	19980312		
EP 713529	A1	19960529	EP 1994-924856	19940809
EP 713529	B1	20000202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1129013	A	19960814	CN 1994-193027	19940809
HU 74271	A2	19961128	HU 1995-3853	19940809
HU 219504	B	20010428		
JP 09501053	T2	19970204	JP 1994-506226	19940809
AT 189475	E	20000215	AT 1994-924856	19940809
ES 2142953	T3	20000501	ES 1994-924856	19940809
RU 2157406	C2	20001010	RU 1996-104372	19940809
CZ 288795	B6	20010912	CZ 1996-357	19940809
ZA 9405992	A	19950314	ZA 1994-5992	19940810
US 5994094	A	19991130	US 1994-288508	19940810
TW 448183	B	20010801	TW 1994-83108337	19940909

L5 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1996:732173 CAPLUS
DN 126:1703
TI Recombinant preparation of dimeric human protein **MP52** and use for treating **bone** diseases
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
IN Makishima, Fusao; Takamatsu, Hiroyuki; Miki, Hideo; Kawai, Shinji; Kimura, Michio; Matsumoto, Tomoaki; Katsuura, Mieko; Enomoto, Koichi; Satoh, Yusuke
AB Methods for recombinant prepn. of mature monomeric human protein **MP52** (119 amino acids) in transgenic Escherichia coli followed by chem. dimerization of the protein are disclosed. Biol. effects of the dimer on stimulating the growth of **bones** or **cartilage**

were also demonstrated. This dimer protein is useful in the treatment of **cartilage** and **bone** diseases.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9633215	A1	19961024	WO 1996-JP1062	19960419
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2216741	AA	19961024	CA 1996-2216741	19960419
AU 9653470	A1	19961107	AU 1996-53470	19960419
AU 704515	B2	19990422		
CN 1187824	A	19980715	CN 1996-194702	19960419
EP 955313	A1	19991110	EP 1996-910198	19960419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
BR 9608019	A	19991130	BR 1996-8019	19960419
JP 2997549	B2	20000111	JP 1996-531621	19960419
NO 9704812	A	19971219	NO 1997-4812	19971017
US 2002102633	A1	20020801	US 1997-945459	19971209

L5 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1997:574505 CAPLUS
DN 127:258055
TI Manufacture of **bone** morphogenetic proteins 12 and 13 and morphogenetic protein **MP52** for use in the induction of tendon or ligament formation and wound repair
SO U.S., 43 pp., Cont.-in-part of U.S. Ser. No. 164,103, abandoned.
CODEN: USXXAM
IN Celeste, Anthony J.; Wozney, John M.; Rosen, Vicki A.; Wolfman, Neil M.; Thomsen, Gerald H.; Melton, Douglas A.
AB Methods of manuf. of **bone** morphogenetic proteins 12 and 13 and the morphogenetic protein **MP52**, or biol. active peptides derived from them for use in the stimulation of tendon and ligament formation in the stimulation of wound repair are described. The manuf. of biol. active human BMP12 in bacterial and animal expression systems is described. The material manufd. in animal cells as a fusion protein with the propeptide of BMP2 was biol. active in the Rosen-modified Sampath-Reddi assay.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5658882	A	19970819	US 1994-362670	19941222
US 6027919	A	20000222	US 1994-333576	19941102
US 6284872	B1	20010904	US 1997-808324	19970228
US 6187742	B1	20010213	US 1999-274575	19990323

L5 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1998:542980 CAPLUS
DN 129:140696
TI Freeze-dried composition of **bone** morphogenetic protein human **mp52**
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
IN Inagaki, Mitsuko; Ichikawa, Hideki
AB The invention relates to a stable freeze-dried compn. of a **bone** morphogenetic protein human **MP52** wherein coloration and shrinking of **MP52** during storage and aggregation at the re-dissoln. can be prevented. The compn. is obtained by mixing **MP52** with mannitol at a wt. ratio of 1 : 5 to 1 : 50 followed by freeze-drying.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9833514	A1	19980806	WO 1998-JP371	19980129
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,				

GA, GN, ML, MR, NE, SN, TD, TG

AU 9856791	A1	19980825	AU 1998-56791	19980129
AU 737595	B2	20010823		
EP 972520	A1	20000119	EP 1998-901044	19980129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9807537	A	20000321	BR 1998-7537	19980129
NO 9903702	A	19990929	NO 1999-3702	19990729

L5 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS
AN 1999:764189 CAPLUS
DN 132:9630
TI Expression of mutant recombinant human **MP52** protein monomer with **bone** morphogenetic activity and its use for preventing and treating **cartilage** and **bone** diseases
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
IN Kawai, Shinji; Kimura, Michio; Muraki, Yoshifumi; Katsuura, Mieko
AB A mutant recombinant human **MP52** protein monomer belonging to TGF-.beta. superfamily with two-fold higher activity for inducing osteoblast cell line differentiation was created by site-directed mutagenesis replacing a cysteine contributing to dimer formation with another amino acid. Another amino acid replacing a cysteine can be serine, threonine, alanine, or valine, and preferably alanine. The mutant recombinant protein can be expressed in Escherichia coli, yeast, insect cells, and mammalian cells that have been transformed with an expression vector having a DNA sequence coding for the monomer protein. The use of the mutant recombinant human **MP52** protein monomer for prevention and therapeutic treatment of **bone** and/or **cartilage** diseases such as osteoporosis, osteoarthritis or arthrosteitis, **bone** fracture, and lack of teeth root or tooth socket is claimed.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9961611	A1	19991202	WO 1999-IB866	19990514
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 11335398	A2	19991207	JP 1998-141379	19980522
AU 9935309	A1	19991213	AU 1999-35309	19990514
EP 1078054	A1	20010228	EP 1999-917029	19990514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002516098	T2	20020604	JP 2000-550995	19990514

=>

L Number	Hits	Search Text	DB	Time stamp
7	70	MP52 and bone	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:22
13	40	(MP52 and bone) and matri$10	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:46
19	3	(MP52 and bone) and crystal$8	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:49
25	10	crystallographically WITH calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:51
31	8	MP52 and MP52.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:54
55	3462	424/93.$2.ccls.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:55
67	250	424/93.$2.ccls. and bone.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:56
79	147	(424/93.$2.ccls. and bone.clm.) and matrix	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:57
85	103	((424/93.$2.ccls. and bone.clm.) and matrix) and (calcium or tricalcium)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:57
91	22	(424/93.$2.ccls. and bone.clm.) and (matrix WITH (calcium or tricalcium))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 12:58
121	12	PAULISTA NEAR MICHAEL	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:08
137	1067	bone ADJ morphogenic ADJ protein	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:14
143	2	(bone ADJ morphogenic ADJ protein) and (calcium NEAR matrix)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:14
1	105	MP52	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:21
149	36	(MP52 and bone) and calcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:22
155	37	(MP52 and bone) and (calcium or tricalcium)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:24
161	26	((MP52 and bone) and (calcium or tricalcium)) and pure	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:25

167	330	alpha-tricalcium or beta-tricalcium	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:29
173	6	(alpha-tricalcium or beta-tricalcium) WITH matrix	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:26
185	116	(alpha-tricalcium or beta-tricalcium) and bone.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:30
191	108	((alpha-tricalcium or beta-tricalcium) and bone.clm.) and (matrix or composition or support)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:52
197	8	((424/93.$2.ccls. and bone.clm.) and (matrix WITH (calcium or tricalcium))) and pure	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:54
203	0	((424/93.$2.ccls. and bone.clm.) and (matrix WITH (calcium or tricalcium))) and phase-pure	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/15 13:54

US 20020045568A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2002/0045568 A1**

HOTTEN et al. (43) **Pub. Date: Apr. 18, 2002**

(54) **USE OF MP52 0R MP121 FOR TREATING AND PREVENTING DISEASES OF THE NERVOUS SYSTEM**

(76) Inventors: **GERTRUD HOTTEN**, HERNE (DE); **JENS POHL**, HAMBRUCKEN (DE); **ROLF BECHTOLD**, HEIDELBERG (DE); **MICHAEL PAULISTA**, LEIMEN (DE); **KLAUS UNSICKER**, HEIDELBERG (DE)

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(*) Notice: This is a publication of a continued prosecution application (CPA) filed under 37 CFR 1.53(d).

(21) Appl. No.: **08/981,490**

(22) PCT Filed: **Jul. 12, 1996**

(86) PCT No.: **PCT/EP96/03065**

(30) **Foreign Application Priority Data**

Jul. 12, 1995 (DE)..... 195 25 416 .3

Publication Classification

(51) **Int. Cl.**[7] **A61K 38/16**; C07K 14/435; A61K 38/00

(52) **U.S. Cl.** **514/2**; 514/12; 530/350

(57) **ABSTRACT**

The present invention concerns the use of biologically active MP52 or/and MP121 for the treatment and prevention of diseases of the nervous system or/and for the treatment of neuropathological situations which are caused by ageing of the nervous system. A pharmaceutical agent according to the invention for the treatment and prevention of diseases of the nervous system or/and for treating neuropathological situations which are caused by ageing of the nervous system therefore contains biologically active MP52 or/and MP121 as the active substance.

US006120760A

United States Patent [19]

Hötten et al.

[11] **Patent Number: 6,120,760**

[45] **Date of Patent: Sep. 19, 2000**

[54] **GROWTH/DIFFERENTIATION FACTORS OF THE TGF-β FAMILY**

[75] Inventors: **Gertrud Hötten**, Bammental; **Helge Neidhardt**, Marburg; **Rolf Bechtold**, Heidelberg; **Jens Pohl**, Hambrücken, all of Germany

[73] Assignee: **Biopharm Gesellschaft zur Biotechnologischen Entwicklung**, Heidelberg, Germany

[21] Appl. No.: **08/289,222**

[22] Filed: **Aug. 12, 1994**

Related U.S. Application Data

[63] Continuation-in-part of application No. PCT/WO93/16099, Feb. 12, 1993.

[30] **Foreign Application Priority Data**

Feb. 12, 1992 [EP] European Pat. Off. 92102324
Jul. 1, 1994 [DE] Germany 44 23 190

[51] **Int. Cl.**[7] **A61K 38/19**; C07K 14/495; C12N 15/19

[52] **U.S. Cl.** **424/85.1**; 530/351; 536/23.1; 536/23.5; 536/24.3; 536/24.31; 514/2; 514/8; 514/12; 435/69.5; 435/325; 435/471; 435/252.3; 435/320.1

[58] **Field of Search** 424/85.1; 435/69.5, 435/112.3, 471, 325, 252.3, 320.1; 514/2, 8, 12; 536/23.1, 23.5, 24.3, 24.31; 530/351

[56] **References Cited**

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5,801,014 9/1998 Lee et al. 435/69.1

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0 222 491 10/1986 European Pat. Off. .
93/16099 PCT/EP 8/1993 WIPO .
94/02552 11/1995 WIPO .

OTHER PUBLICATIONS

Chang et al. (1994). J. Biol. Chem. vol. 269, No. 45, pp. 28227–28234.

Hötten et al., "Cloning of a New Member of the TGF–β Family: A Putative New Activin β_C Chain", *Biochem. & Biophys. Res. Comm.*, vol. 206, No. 2, 1995.

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[57] **ABSTRACT**

The invention provides DNA sequences encoding novel members of the TGF-β family of proteins. The TGF-β family comprises proteins which function as growth and/or differentiation factors and which are useful in medical applications. Accordingly, the invention also describes the isolation of the above-mentioned DNA sequences, the expression of the encoded proteins, the production of the proteins and pharmaceutical compositions containing the proteins.

12 Claims, 3 Drawing Sheets

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

TAAATCTTGG GACACGCAGC A 21

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

CAGGTCCTGG GGCACGCAGC A 21

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

CCCTGGGAGA GCAGCACAGC A 21

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

CAGCTTGGTG GGCACACAGC A 21

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

CAGCTTGGTG GGAATGCAGC A 21

We claim:

1. An isolated protein of the TGF-β family encoded by a DNA comprising a nucleotide sequence selected from the following group:

(a) the nucleotide sequence as shown in SEQ ID NO:1,

(b) a nucleotide sequence which is degenerate as a result of the genetic code to the nucleotide sequence of (a), and

(c) fragments of (a) or (b) which encode a protein which has essentially the same cartilage or bone inducing activities as a mature protein encoded by the nucleotide sequence of SEQ ID NO:1.

2. A protein according to claim 1 comprising the amino acid sequence of SEQ ID NO: 3.

3. The protein of claim 1 wherein the DNA is a mammalian DNA.

4. The protein of claim 1 wherein the DNA comprises the nucleotide sequence shown in SEQ ID NO. 1.

5. An isolated mature protein, wherein said protein is encoded by the nucleotide sequence of SEQ ID NO:1.

6. A composition containing a protein of the TGF-β family according to any one of claims 1, 2, 3, 4, 5 in combination with an acceptable carrier.

7. A method for the treatment of bone and cartilage defects comprising administering a composition containing a protein of the TGF-β family according to claim 6.

8. An isolated MP-121 protein of the TGF-β family encoded by a DNA comprising a nucleotide sequence selected from the following group:

(a) the nucleotide sequence as shown in SEQ ID NO:2,

(b) a nucleotide sequence which is degenerate as a result of the genetic code to the DNA of (a),

(c) a nucleotide sequence which hybridizes under the following stringent hybridization conditions to the DNA in (a), or (b): hybridization at a salt concentration of 4X SSC at 62°–66° C. followed by a one-hour wash with 0.1X SSC and 0.1% SDS at 62°–66° C., and

(d) fragments of (a), (b) or (c) which encode a protein which has essentially the same cartilage or bone inducing activity as a mature protein encoded by the nucleotide sequence of SEQ ID NO:2.

9. A protein according to claim 8 comprising the amino acid sequence of SEQ ID NO: 4.

10. The protein of claim 8, wherein the DNA comprises the nucleotide sequence shown in SEQ ID NO: 2.

11. The protein according to claim 8, wherein said protein contains the amino acid sequence Leu-Leu-Lys-Ala-Asn-Thr-Ala-Ala-Gly Thr (SEQ ID NO:10) and is at least 116 amino acids long.

12. An isolated mature protein, wherein said protein is encoded by the nucleotide sequence of SEQ ID NO:2.

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